Statement of

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am William K. Hubbard, Senior Associate Commissioner for Policy, Planning and Legislation, Food and Drug Administration (FDA or the Agency). I appreciate the opportunity to discuss our mutual concerns related to the importation of drugs into the United States. This topic encompasses a range of issues, including the importation by individuals of prescription drugs at land borders or through the mail; the introduction into the U.S. of controlled substances from foreign sources under the guise of personal importation; the potential introduction of counterfeit bulk drugs into the U.S. drug supply; and the purchase of drugs from foreign sources over the Internet. Let me begin by discussing one of our greatest challenges in this area.

PERSONAL IMPORTATION OF DRUGS THROUGH THE MAIL

The amount of prescription drugs for personal use imported through the mail has increased in recent years. According to testimony by the U.S. Customs Service (Customs) before the Government Reform Committee in May of last year, seizures of parcels containing scheduled or controlled substances at international mail facilities increased by 450 percent in FY 1999, primarily due to drug sales over the Internet. We estimate that approximately two million parcels containing FDA-regulated products for personal use enter the U.S. each year through international mail facilities that Customs could set aside for FDA review for possible violations of the Federal Food, Drug, and Cosmetic (FD&C) Act. This estimate is based on an

extrapolation of data obtained during a pilot project conducted at the international mail facility in Carson, California (see below).

Under the FD&C Act, unapproved, misbranded, and adulterated drugs are prohibited from importation into the U.S., including foreign versions of U.S.-approved medications, as is reimportation of approved

drugs made in the U.S. In general, all drugs imported by individuals fall into one of these prohibited categories.

From a public health standpoint, importing prescription drugs for personal use is a potentially dangerous practice. FDA and the public do not have any assurance that unapproved products are effective or safe, or have been produced under U.S. good manufacturing practices.

U.S.-made drugs that are reimported may not have been stored under proper conditions, or may not be the real product, because the U.S. does not regulate foreign distributors or pharmacies. Therefore, unapproved drugs and reimported approved medications may be contaminated, subpotent, superpotent, or counterfeit. In addition, some foreign websites offer to prescribe medicines without a physical examination, bypassing the traditional doctor-patient relationship. As a result, patients may receive inappropriate medications because of misdiagnoses, or fail to receive appropriate medications or other medical care, or take a product that could be harmful, or fatal, if taken in combination with other medicines they might be taking.

Personal Importation Policy

Under FDA's personal importation policy, as described in guidance to the Agency's field personnel, FDA inspectors may exercise enforcement discretion to permit the importation of certain unapproved prescription medication for personal use.

First adopted in 1954, the policy has been modified several times over the succeeding years. It was last modified in 1988, in response to concerns that certain potentially effective treatments for AIDS patients were not available in the U.S., but were available in other countries. The Agency expanded the guidance for humanitarian purposes to allow individuals suffering from serious medical conditions to acquire medical treatments legally available in foreign countries but not approved in the U.S.

The current policy permits the exercise of enforcement discretion to allow entry of an unapproved prescription drug if:

- the product is for personal use (a 90-day supply or less, and not for resale);
- the intended use is for a serious condition for which effective treatment may not be available domestically (and, therefore, the policy does not permit inspectors to allow foreign versions of U.S.-approved drugs into the U.S.);
- there is no known commercialization or promotion to U.S. residents by those involved in the distribution of the product;
- the product is considered not to represent an unreasonable risk; and

- the individual seeking to import the product affirms in writing that it is for the patient's own use and provides the name and address of the U.S. licensed doctor responsible for his or her treatment with the product or provides evidence that the product is for the continuation of a treatment begun in a foreign country.

FDA has not officially permitted the importation of foreign versions of U.S.-approved medications, even if sold under the same name, because these products are unapproved, and the Agency has no assurance that these products are safe or effective, while safe and effective versions are already available in the U.S.

FDA believes that the need for its personal importation policy is far less now than it was when the current version of the policy was developed in 1988. Now, due to faster review times and various regulatory mechanisms through which patients can obtain unapproved treatments for humanitarian purposes, the need to import therapies not available in the U.S. has diminished. According to a Tufts University study presented in September 2000, 80 percent of new molecular entities approved in the U.S. in 1996 through 1998 received that approval within a year of its first introduction on the world market, almost double the rate during the years 1991 through 1995.

Implementation of the Personal Importation Policy

At mail facilities, Customs officials identify parcels that may be violative of the FD&C Act. FDA inspectors then determine if these products should or should not be permitted to enter the country. If detained, FDA must issue a notice to the addressee describing the potential Federal violation and provide the individual with an opportunity to respond. If the addressee does not respond or provides an inadequate response, FDA will give the parcel back to Customs to have it returned to the exporter. Due to the requirements for notice and the opportunity to respond, the process for detaining and further processing mail parcels consumes large amounts of FDA resources. In addition, much storage space would be needed to hold the large number of detained parcels pending replies from the addressees.

FDA's personal importation policy, as written, is difficult to implement. This is due, at least in part, to the difficulty faced by FDA inspectors, or even health care practitioners, in identifying a medicine by its appearance, and labeling may falsely identify a product. From a practical standpoint, FDA inspectors

cannot examine drug products contained in a mailed parcel and accurately determine the identity of such drugs or the degree of risk posed to the individual who will receive these drugs.

FDA detains and refuses few mail imports for personal use. As a consequence, the tens of thousands of parcels that FDA does not review are eventually released by Customs and sent on to their addressees, even though the products contained in these parcels may appear to violate the FD&C Act and may pose a health risk to consumers. We do not believe this is an acceptable public health outcome and are working to develop a solution.

HHS Plan to Address Mail Imports for Personal Use

Due to the inability of FDA to cope with the volume of medications imported for personal use through the mail, and because of the public health risks associated with these products (as discussed below), FDA has been working to develop a more effective personal importation policy. In addition, we recognize that Customs is dependent on guidance from FDA, and one of our goals is to provide clear and simple standards for assessing parcels containing drug products. We are discussing options for revisions to the Agency's personal importation policy with Secretary Thompson.

CARSON MAIL FACILITY PILOT

Earlier this year, FDA and Customs conducted a survey of imported drug products entering the U.S. through the Carson City, California mail facility (the Carson pilot). The Carson pilot was proposed by Customs as a means to examine incoming mail shipments of pharmaceutical products over a specified time frame in order to identify both the volume and the types of drug products entering the U.S. We also hoped to better assess the efforts required to cover drug importations at a mail facility, and to gain

a better understanding of the public health implications these importations may have for U.S. consumers.

The Carson pilot ran for a five-week period, with FDA inspectors present for 40 hours per week. At the onset, Customs took a "baseline" sample in the first week by setting aside all international packages that were suspect, or that they would have set aside for FDA review had FDA been able to process them. The number of packages set aside was approximately 3,300. Multiplying that number by five weeks provides an estimated total of 16,500 international packages (650 packages per day) that Customs could have set aside for FDA review during the Carson pilot, if the ability to process them was not a factor. After the first week, however, Customs actually set aside the number of packages they believed FDA would be able to examine. In general, during each week of the Carson pilot, more packages were set aside than FDA was able to handle.

FDA was actually able to examine 1,908 packages during the five-week pilot, an average of approximately 381 packages per week. Neither FDA nor Customs kept a count of the packages that were set aside but not examined. Unexamined packages were sent on to the addressees.

Of the 1,908 packages examined by FDA, 721 parcels were detained and the addressees notified that the products appeared to be unapproved for use in the U.S., misbranded and/or a drug requiring a doctor's prescription. The parcels were shipped from a total of 19 countries, and overall, there was no obvious evidence of the products being imported for further commercial distribution. On average, the Agency was detaining at a rate of 144 packages per week, or about 38 percent of those examined.

Clearly, the Carson pilot demonstrated that the rate of packages coming into the U.S. exceeds FDA's capacity to manage, thus, Customs is left with little choice but to forward the majority of packages to addressees. As we stated, we do not believe this is an acceptable public health outcome, and we are working to develop a solution.

Analysis of the Carson Pilot Drug Parcels

In order to define better the nature of the risk to public health from the types of products coming into the U.S. through personal importation, FDA's Center for Drug Evaluation and Research (CDER) reviewed listings of the products detained during the Carson pilot. CDER's review demonstrates that there are serious public health risks associated with many of the 721 drug shipments (composed of 197 different drugs) intercepted at Carson. In general, there are two types of risks that consumers of these drugs would face. The first type of risk is that associated with taking drugs of unknown origin or quality. Second are the very significant risks associated with taking many of these drugs without first obtaining a physician's prescription and without the continued oversight of the physician.

Risks Associated with Drugs of Unknown Origin or Quality

In general, FDA has no information to establish where these drugs were actually manufactured and whether necessary current Good Manufacturing Practice requirements were followed. There is also no assurance that the drugs were packaged and stored under appropriate conditions to avoid degradation or contamination.

Approximately eight percent of the shipments contained drugs that could not be identified because they contained no labeling; some of these contain only foreign language labeling. Most of these drug shipments were contained in plastic bags; one shipment contained drugs taped between magazine pages.

Several drugs do not appear to correspond with any U.S.-approved drugs and the risks are therefore difficult to assess. One drug was evaluated for FDA approval but was denied approval. This drug is associated with cardiac abnormalities and its efficacy could not be successfully demonstrated. Another drug approved abroad but not in the U.S. is associated with medically serious gastro-intestinal

complications. Several shipments contained three drugs that were once approved by FDA but have been withdrawn from the market based on serious safety concerns, including:

- fatal arrhythmia and dangerous drug interactions;
- loss of white blood cells (agranulocytosis) associated with fatal infections; and
- hemorrhagic stroke.

Risks Associated with the Absence of Physician Oversight

The vast majority of the shipments were identified as containing prescription drugs, which by definition, have serious toxicities and risks associated with them such that they are "not safe for use except under the supervision of a practitioner licensed by law to administer such drug." (Title 21, United States Code, section 353(b)). Although some foreign Internet sites might offer an online questionnaire, we believe that very few, if any, require a prescription from a practitioner licensed in the U.S. before dispensing such drugs to U.S. residents. Moreover, after detention notices were issued to the intended recipients of the 721 drug shipments, fewer than four percent presented evidence of prescriptions to document their relationship with a physician in association with the drugs purchased from abroad. The lack of adequate English language labeling accompanying many of these shipments exacerbates the risks associated with the absence of physician oversight.

During the Carson pilot, as in normal practice, Customs generally separated out controlled substances for processing by the Drug Enforcement Administration (DEA) before the remaining shipments were provided for FDA review. However, in FDA's review, six controlled substances were identified, including lorazepam, codeine sulfate, loperamide, chlordiazepoxide, chloral hydrate, and diphenoxylate. These drugs have the potential to cause addiction or be abused. Life-threatening overdoses are possible. A physician's prescription and oversight are essential for managing these risks.

There are numerous drugs identified on the Carson list that are intended to treat conditions that

consumers need physicians to properly diagnose. As a result, consumers who bypass physician diagnosis and prescribing may be exposing themselves to risks and toxicities that cannot be justified by offsetting benefits to those patients.

- For example, almost ten percent of the shipments were for antibiotics, despite the fact that consumers are generally not able to diagnose whether their symptoms are caused by bacterial infections. The overuse of antibiotics continues to be a serious public health concern because it is linked to the growth of antibiotic resistant-bacteria.
- Several drugs listed are potent steroids, which are generally prescribed for conditions that are not self-diagnosable. In addition, potential adverse events associated with these

  drugs, including diabetes, hypertension, and serious infection require prompt attention and careful monitoring.

There are many drugs on the list for which it is essential that the proper dose be delivered into the bloodstream at the proper rate. Some of these drugs have a narrow range in which they can safely achieve their therapeutic effect. At least seven such drugs were identified on the Carson list. Without FDA oversight, there is the risk that these drugs may not have been manufactured with the necessary quality controls to ensure a consistently safe and effective product.

- One seizure medication on the Carson list, for which there were three shipments, could be very dangerous if not manufactured to these rigorous standards. Any change in potency could render the drug ineffective or highly toxic.
- Another seizure drug on the list for which physician monitoring is also essential has a narrow therapeutic range and FDA labeling provides a black-box warning for hepatoxicity, teratogenicity, and pancreatitis.

More than 30 drugs on the list have serious contraindications and/or drug interactions for which physician oversight is essential. For instance, almost 20 percent of the shipments were for various estrogen products for which there are multiple serious contraindications that a physician needs to consider before making prescribing decisions and in monitoring the patient.

It is impossible to make a scientifically definitive statement on the public health impact of the drug shipments encountered during the Carson pilot without extensive chemical testing and analysis of the incoming pharmaceuticals, which would be prohibitively expensive. Based on the observations noted above, however, FDA believes that these drugs pose substantial risks to the public health, and we further believe that significant changes to the policies governing personal importations through the mail are warranted.

BORDER SURVEYS

Over the last year, FDA has initiated three other surveys to gather data on drug products imported by individuals into the U.S. Although these border surveys involve land traffic rather than mail importation, the results of these surveys show some similarities to the findings from the Carson mail pilot, as well as some significant differences.

Southwest Border Survey (August 2000)

A survey of prescription drugs being brought by pedestrians into the U.S. at eight ports of entry along the 2,000 mile border with Mexico was conducted by FDA's Southwest Import District (SWID) with the assistance of other agencies including Customs, the DEA, the U.S. Department of Agriculture, and others. The survey looked at activity during four hours on a Saturday (August 12, 2000) at eight border ports in California, Arizona, and Texas. The purpose of the survey was to interview individuals walking across the border into the U.S. from Mexico who

had purchased prescription drugs in Mexico to determine 1) what specific types of products are being imported, and 2) who is importing these products.

The data collected from over 600 interviews indicated that the most common importer of prescription drugs during the survey was an older male Caucasian with a prescription from the U.S., bringing back primarily antibiotics or pain relievers for his own use. Prescriptions were held by 63 percent of the persons interviewed (59 percent U.S. prescriptions and 41 percent Mexican). The most common drugs and their indications that were purchased in Mexico during the survey were as follows: Amoxicillin (antibiotic), Glucophage (diabetes), Premarin (estrogen), Dolo Neurobion (vitamin supplement), Vioxx (inflamation), Retin-A (acne), Tafil (anxiety), Celebrex (arthritis), Penicillin (antibiotic), Viagra (impotence), Carisoprodal (analgesic).

Canadian Border Survey

On January 6, 2001, in cooperation with Customs, FDA conducted a survey to obtain a snapshot of prescription drug products being brought into the U.S. from Canada via passenger vehicles. During the eight-hour survey at three ports of entry in New York, Michigan and Washington, a total of 10,374 passenger vehicles and 58 buses crossed into the U.S. Of these, 33 passenger vehicles (35 individuals) were referred by Customs to be interviewed. These individuals brought in a total of 47 containers of drug products from Canada.

The types of products included pain medicines -- primarily "222" (a combination of acetaminophen, caffeine, and codeine) or similar products. The indicated reason for import was

that the products were available over-the-counter (OTC) in Canada and cost less than in the U.S. The

next largest group of products was herbal products, with the reason for importation being that the products were not available in the U.S. Other products included Tobradex (antibiotic/steroid opthalmic for individuals having laser eye surgery); Claritin and Allegra (allergies) purchased OTC in Canada; Sibelium capsules (calcium channel blocker); and a variety of OTC products sold in Canada and not available in the U.S.

Southwest Border Survey (April 2001)

On April 11, 2001, FDA, Customs, and other agencies conducted a survey of prescription drugs being brought into the U.S. at seven ports of entry along the U.S./Mexican border. This survey coincided with both Easter vacations from many colleges and the end of the "snowbird" season, when tourists from Northern states visiting along the Southern border return home.

During the four hour "blitz" a total of 586 persons brought in a total of 1,120 drugs. Approximately 56 percent had a prescription for the medicines (61 percent were U.S. prescriptions, 39 percent were Mexican). The most common drugs purchased in Mexico were: Amoxicillin (antibiotic), Premarin (estrogen), Claritine (allergy), Terramicinia (antibiotic), Ampicillin (antibiotic), Ibuprofen (analgesic), Penicillin (antibiotic), Vioxx (inflammation), Tafil (anxiety), Dolo Neuorobian (vitamin supplement), Glucophage (diabetes), Celebrex (arthritis), Naproxen (analgesic), Retin-A (acne), Ventolin (pulmonary disease), and Valium (controlled substance/nervous system depressant).

CONTROLLED SUBSTANCES

Although we do not know, nor is it possible to clearly determine, the amount of controlled substances brought into the U.S. purportedly for personal use, it is likely that such medicines are frequently imported for resale and pose a public health risk. The Agency has been working with both Customs

and DEA to streamline and clarify Federal import policies specifically related to the importation of controlled substances.

INTERNET DRUG SALES

Based on surveys conducted in early 2000 by Office of Criminal Investigations (OCI) and subsequently by the General Accounting Office (GAO), it appears that there are roughly 300 to 400 Internet sites selling prescription drugs, with approximately half located domestically and half located outside the U.S. FDA has long taken the position that consumers are exposed to a number of risks when they purchase drugs from Internet sites or other mail order outlets that dispense foreign drugs. These outlets may dispense expired, subpotent, contaminated or counterfeit product, the wrong product, a contraindicated product, an incorrect dose, or medication unaccompanied by adequate directions for use. FDA cannot provide consumers with any assurance that these products were manufactured under current good manufacturing practice standards. Taking an unsafe or inappropriate medication puts consumers at risk for dangerous drug interactions and other serious health consequences.

Internet sites that provide prescription drugs by having consumers fill out a questionnaire rather than seeing a doctor pose serious health risks. A questionnaire generally does not provide sufficient information for a healthcare professional to determine if that drug is appropriate or safe to use, if another treatment is more appropriate, or if the consumer has an underlying medical condition where using that drug may be harmful.

FDA has undertaken widespread public relations efforts to warn consumers about the dangers of buying drugs online, and we have provided extensive information on these dangers on FDA's own Internet site. FDA's Buying Medical Products Online web page is one of the most frequently requested pages on FDA's website. It consistently ranks among the top twenty requested pages, averaging almost 13,000

hits per month.

Currently, FDA has 90 sites under active review for possible regulatory or civil action. Warning letters have been sent to 48 domestic online sellers. Additionally, FDA has sent 121 "cyber letters" to operators of Internet sites offering to sell online prescription drugs or unapproved drugs. These sites may be engaged in illegal activity such as offering to sell prescription drugs to U.S. citizens without valid (or in some cases without any) prescriptions. Cyber letters are sent over the Internet to the suspect websites to warn the operators that they may be engaged in illegal activities, and inform them of the laws that govern prescription drug sales in the U.S. Cyber letters have a deterrent effect and FDA has seen positive results from using them. FDA has received positive responses from 20 percent of the cyber letter recipients and we are continuing to monitor these sites.

FDA also sends copies of its cyber letters to the home governments of targeted websites, when the locations can be identified. Follow-up depends on the ability and willingness of the foreign regulatory bodies to investigate and take actions against website operators who are illegally shipping drugs to other countries.

In cooperation with the Department of Justice (DOJ), five preliminary injunctions have been imposed on the sale of a illegal products, including one product marketed as a weight-loss aid containing a potent thyroid hormone which could cause heart attacks or strokes, and an unapproved cancer therapy. FDA and DOJ also are pursuing an injunction against the sale of another unapproved cancer therapy over the Internet. Additionally, 15 product seizures, 11 product recalls, and the voluntary destruction of 18 violative products have been achieved, generally pertaining to unapproved new drug products including gamma hydroxybutyric acid, gamma butyrolactone , Triax, 1,4 butanediol, and laetrile. Thirty-six foreign shippers have been placed on Detention Without Physical Examination and added to Import Alert 66-57 for targeting sales of unapproved new drug products to the U.S.

During FY 2001, FDA's OCI initiated approximately 40 Internet-related investigations and will continue to conduct investigations involving suspected criminal activity related to Internet drug sales as well as other Internet-facilitated criminal violations of the FD&C Act. Of the 133 currently open Internet-related investigations, 64 are Internet pharmacy cases, where the focus is on the possible dispensing of prescription drugs without a prescription.

In recent years, OCI has initiated 285 Internet investigations and each of these investigations have involved a variable number of actual websites – typically ranging from one to 25 or more. OCI has effected 88 Internet-related arrests, 70 of these in drug-related investigations. Of the 70 drug-related arrests, 11 have involved Internet pharmacy cases. These arrests have resulted, thus far, in 48 Internet-related convictions, 42 of these in drug-related investigations. Of the 42 drug-related convictions, five have involved cases involving the sale of prescription drugs without a valid prescription.

In addition, OCI has an ongoing initiative at the Dulles International Airport Mail Facility that had its genesis in their first Internet case, which began in 1994. The case, which involved a site selling steroids over the Internet, resulted in a successful prosecution and shutdown of the website. The partnership resulting from this case has continued, and in the past 18 months, OCI has been involved with local law enforcement in the Washington metropolitan area in 98 drug seizures. The seizures represent dozens of types of drugs coming in from 13 different countries. Of the 98 seizures, 87 of the drug seizures were ordered over the Internet and mailed to U.S. citizens; six were mailed to the U.S. by family or friends living abroad; four were ordered via a 1-800 telephone number from Canada and mailed to the U.S.; and one was transported via an airline passenger in two suitcases from Romania. The efforts of OCI, Customs, and local law enforcement have yielded the execution of eight search and seizure warrants and led to the arrest and prosecution of nine people.

CONCLUSION

Mr. Chairman, FDA remains concerned about any possibility that unsafe drugs may find their way into the American drug supply. We will remain vigilant as we refine and improve the programs and procedures that we use to ensure the availability of safe medications for consumers.

We appreciate the Committee interest in assuring that the American public has access to safe and affordable medicines. We look forward to continuing to work with you. Thank you again for the opportunity to participate in today's hearing. I will be happy to answer any questions.